REMARKS

The present application is directed to compositions containing a biologically active agent and a polycationic carbohydrate, wherein the biologically active agent is capable of generating a protective immune response when administered to an animal. Claims 1, 5, 6, 11-17, 20-22 and 37 were pending. Applicants amend dependent Claims 15 and 22 to bring them into correspondence with the base claim, and amend Claim 20 to correct an informality. Applicants add new Claims 44-71. The amendments do not add any new matter. The new claims are based on previously presented claims and are also supported throughout the application, as filed, for example, in the specification on page 9, lines 5-12 and 20-22, page 10, lines 8-25, page 11, lines 7-24, page 13, lines 17-20, page 14, lines 9-24, page 15, lines 17-24, page 20, line 16, through page 21, line 20.

Rejection under 35 U.S.C. §102(b)

Ruprecht et al. (WO 92/05791; "Ruprecht")

The Examiner rejected Claim 1 under 35 U.S.C. §102(b) as anticipated by Ruprecht. Applicants respectfully traverse the rejection.

As provided in MPEP 2131, for anticipation under 35 U.S.C. §102, the reference must teach each and every element of the claim. Applicants assert that Ruprecht fails to teach a pharmaceutical composition comprising an immunostimulating amount of N-carboxymethyl chitosan or a salt thereof.

The Examiner asserts that Ruprecht anticipates Claim 1 because it teaches the sulfated chitosan derivative N-carboxymethyl chitosan-N,O-sulfate. However, N-carboxymethyl chitosan-N, O-sulfate is a different chemical compound that N-carboxymethyl chitosan or a salt thereof, an element of the pending claims. Applicants respectfully submit that Ruprecht fails to teach a pharmaceutical composition comprising N-carboxymethyl chitosan or a salt thereof.

Ruprecht discloses pharmaceutical compositions comprising chitosan derivatives obtained by carboxylation or sulfation for use as therapeutic antiviral agents (see, for example,

Ruprecht, Abstract, page 4, lines 1-10). Ruprecht fails to teach an immunostimulating amount of N-carboxymethyl chitosan as a component of the disclosed pharmaceutical compositions.

Ruprecht discloses N-carboxymethyl chitosan (NCMC) as the starting material for the preparation of N-carboxymethyl chitosan sulfate (NCMCS) (see Ruprecht, page 6, line 20 – page 7, line 15). Ruprecht teaches that NCMS starting material is completely consumed in the reaction described, as confirmed by elemental analysis (see Ruprecht, page 7, line 16, through page 8, line 11). The resulting carboxymethyl chitosan derivative has approximately one sulfate group per sugar residue. On page 9, lines 31-33, Ruprecht confirms that the NCMC starting material is not present in the pharmaceutical compositions described by Ruprecht: "NCMCS does not give a positive ninhydrin reaction, indicating essentially complete N-substitution with N-acetyl, N-carboxymethyl, and/or N-sulfoamino" (emphasis added).

Thus, Ruprecht fails to disclose a pharmaceutical composition comprising an immunostimulating amount of N-carboxymethyl chitosan or any salt thereof and fails to anticipate Claim 1 for at least this reason. Applicants respectfully request withdrawal of the rejection.

Amsden et al. (WO 99/57176; "Amsden")

The Examiner rejects Claims 1, 5-6, 11-15, and 20 under 35 U.S.C. §102(b) as anticipated by Amsden. Applicants respectfully traverse the rejection.

As provided in MPEP 2131, for anticipation under 35 U.S.C. §102, the reference must teach each and every element of the claim. Applicants assert that Amsden fails to teach a pharmaceutical composition comprising an immunostimulating amount of N-carboxymethyl chitosan or a salt thereof. Amsden teaches methods of microsphere production and that the microspheres are suitably formed from a long list of biodegradable polymers, one of which is N-carboxymethyl chitosan (See Amsden, Abstract, page 9, lines 12-26). Amsden teaches that "microspheres can be produced that bear an infectious agent antigen for vaccination" (see Amsden, page 24, lines 1-2). However, Amsden fails to teach microspheres that comprise an immunostimulating amount of N-carboxymethyl chitosan or a salt thereof. Applicants

respectfully assert that Amsden fails to anticipate the rejected claims for at least this reason and request withdrawal of the rejection.

Rejection under 35 U.S.C. §103(a)

MPEP 2142 states: "To reach a proper determination under 35 U.S.C. §103, the examiner must step backward in time and into the shoes worn by the hypothetical 'person of ordinary skill in the art' when the invention was unknown and just before it was made. In view of all the factual information, the examiner must then make a determination whether the claimed invention 'as a whole' would have been obvious at that time to that person." To reject a claim as obvious, the Examiner, first, must resolve the *Graham* factual inquires, namely, (a) determining the scope and content of the prior art, (b) ascertaining the differences between the claimed invention and the prior art, and (c) resolving the level of ordinary skill in the pertinent art. *See* MPEP 2141(II) citing *Graham v. John Deere Co*., 383 U.S. 1 (1966).

Eyles (1998 Vaccine Vol. 16(7):698-707; "Eyles") in view of Amsden

The Examiner rejected Claims 1, 3, 6, 11-17, 20-22, and 37 under 35 U.S.C. §103(a) as obvious over Eyles in view of Amsden. Applicants respectfully traverse the rejection.

Eyles teaches compositions of plague vaccine encapsulated in poly (L-lactide) microspheres. Eyes attempts to improve immunogenicity of microencapsulated Yersinia pestis F1 and V by adjuvantization with CTB, the non-toxic pentameric B subunit of cholera toxin (see Eyles, page 699, first column, second paragraph, page 703, second column, page 705, Table 1). Eyles fails to teach or suggest adding an immunostimulating amount of N-carboxymethyl chitosan to improve immunogenicity of the encapsulated plague vaccine.

Amsden teaches a method for the manufacture of microspheres (see Amsden, page 4, lines 14-18). The goal of Amsden is to provide a simple and reliable method for the large scale production of uniformly-sized microspheres in a continuous fashion (see Amsden page 3, lines 20-27). The method described by Amsden seeks to overcome problems with existing methods for producing microspheres, such as deactivation of encapsulated material, non-uniform particle size and narrow size distribution (See Amsden, page 2, line 20, through page 3, line 19). As

discussed above, Amsden teaches that "microspheres can be produced that bear an infectious agent antigen for vaccination" (see Amsden, page 24, lines 1-2). However, Amsden fails to teach or suggest that immunogenicity of such vaccines can be improved by adding an immunostimulating amount of N-carboxymethyl chitosan or a salt thereof.

Applicants assert that, prior to the applicants' invention of the claimed pharmaceutical compositions, it would not have been obvious one of ordinary skill in the art to select N-carboxymethyl chitosan from the list of polymers suitable for microsphere production taught in Amsden, determine its immunostimulating amount, and combine such an amount with the plague vaccine disclosed in Eyles, in order to arrive at the pending claims. Accordingly, applicants assert that a combination of Amsden and Eyles fails to render the rejected claims obvious and respectfully request withdrawal of the rejection.

Illum (WO 97/20576; "Illum") in view of Amsden

The Examiner rejects Claims 1, 5-6, 11-17, 20-22, and 37 under 35 U.S.C. §103(a) as obvious over Illum in view of Amsden. Applicants respectfully traverse the rejection.

The scope and content of Amsden is discussed in the previous section. Illum teaches the use of chitosans as adjuvants in vaccine compositions, but fails to teach or suggest the use of N-carboxymethyl chitosan as an immunostimulant. Applicants assert that, prior to the applicants' invention of the claimed pharmaceutical compositions, it would not have been obvious to one of ordinary skill in the art to select N-carboxymethyl chitosan from the list of polymers suitable for microsphere production taught in Amsden, determine its immunostimulating amount, and use such an amount with the vaccine compositions disclosed in Illum, in order to arrive at the pending claims. Accordingly, applicants assert that a combination of Illum and Amsden fails to render the rejected claims obvious and respectfully request withdrawal of the rejection.

Duncan et al. (WO 94/20070; "Duncan") in view of Ruprecht

The Examiner rejects Claims 1, 5-6, 11-15, and 20-22 under 35 U.S.C. §103(a) as obvious over Duncan in view of Ruprecht. Applicants respectfully traverse the rejection.

As discussed above, Ruprecht discloses anti-viral pharmaceutical compositions comprising chitosan derivatives obtained by carboxylation or sulfation. Ruprecht fails to teach or suggest pharmaceutical compositions comprising an immunostimulating amount of N-carboxymethyl chitosan (NCMC). Duncan teaches that antigens are more effective when combined with adjuvants and mucoadhesives. Duncan fails to teach or suggest that the use of chitosans and, more specifically, of N-carboxymethyl chitosan, to improve the immunogenicity of antigens.

Thus, Duncan is silent on the use of N-carboxymethyl chitosan in a pharmaceutical composition and Ruprecht teaches N-carboxymethyl chitosan sulfate prepared from N-carboxymethyl chitosan is effective as an anti-viral agent (see Ruprecht, page 12, lines 1-28). Applicants respectfully submit that Ruprecht would have led a person of ordinary skill in the art in the field of the present application to not use N-carboxymethyl chitosan, since Rupert directs one of ordinary skill in the art to use its therapeutically effective sulfated derivate.

Applicants assert that, prior to the applicants' invention of the claimed pharmaceutical compositions, it would not have been obvious to one of ordinary skill in the art in the field fo ther present application to use N-carboxymethyl chitosan, which is taught in Ruprecht as a starting material for production of a derivative therapeutically effective compound, determine its immunostimulating amount, and combine such an amount with the vaccine compositions disclosed in Duncan, in order to arrive at the pending claims. Accordingly, applicants assert that a combination of Duncan and Ruprecht fails to render the rejected claims obvious and respectfully request withdrawal of the rejection.

CONCLUSION

This Response fully addresses the rejections in the Final Office Action mailed August 13, 2008. Based upon the amendments and remarks provided above, applicants believe that the pending claims are in condition for allowance. A Notice of Allowance is therefore respectfully solicited.

No additional fees are believed due; however, the Commissioner is hereby authorized to charge any additional fees that may be required, or credit any overpayment, to Deposit Account No. 11-0855.

If the Examiner believes any informalities remain in the application that may be corrected by an Examiner's Amendment, or that there are any other issues that can be resolved by a telephone interview, a telephone call to the undersigned attorney at (404) 815-6102 is respectfully solicited.

Respectfully submitted,

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